UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,231	04/21/2006	John Nicholas Staniforth	478.1072	8836

23280 7590 02/04/2009

Davidson, Davidson & Kappel, LLC
485 7th Avenue
14th Floor
New York, NY 10018

EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,231	STANIFORTH ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35 and 42-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 42-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/06/05* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/05, 03/06/07, 09/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-35 and 42-47 are currently pending in the application.

Applicant's election of Group I (i.e. composition) in the reply filed on 12/04/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

Claims 1-35 and 42-47 are examined on the merits herein.

Provisional Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 11-14, 19, 22-23 and 27-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of copending Application No. 10/413022 (hereinafter Staniforth US Patent Application No. '022). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a composition comprising apomorphine or its pharmaceutically acceptable salt or ester and a carrier. The claimed invention and co-pending application Staniforth '022 are rendered obvious over another as the claimed invention teaches its treatment as useful for the treatment of sexual dysfunction whereas Staniforth '022 teaches particular dosages of the composition. Thus, the aforementioned claims of the instant application

are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 10/413022.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-2, 10-18, and 23-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 16, and 30-33 of copending Application No. 10/621964 (hereinafter Staniforth US Patent Application No. '964). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a composition or a method containing a composition comprising apomorphine or its pharmaceutically acceptable salt or ester. The claimed invention and co-pending application Staniforth '964 are rendered obvious over another as the claimed invention teaches a composition for pulmonary inhalation comprising apomorphine, its pharmaceutically acceptable salt or ester whereas Staniforth '694 teaches a method for treating sexual dysfunction comprising a similar composition comprising particular dosages of apomorphine. While Staniforth '694 is directed to a method, such method however necessarily uses a similar composition rendering the instant application obvious. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 10/621964.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Gupta et al. (U.S. 2002/0006933 A1, previously cited by applicant and filed on an IDS 1449).

It is respectfully pointed out that the recitation "for treating sexual dysfunction by pulmonary inhalation" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robbie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Gupta et al. teach a method for administering apomorphine to a patient for the treatment of sexual dysfunction while reducing undesirable side effects and wherein the apomorphine is attained with the patient's plasma of up to 10 ng/ml (see abstract and pg.1, paragraphs 0001 and 0011-0012). Gupta et al. further teach that the method of administration can be by inhalation to the lungs (see pg. 1, paragraphs 0012 and 0020 and pg. 2, paragraph 0033). Additionally, Gupta et al. disclose that the method may be utilized to treat sexual dysfunction in males or females and that the plasma concentration of apomorphine (i.e. Cmax) may be from about 0.1 to about 7 ng/ml (instant claims 4-5; see pg. 2, paragraph 0023). Gupta et al. further teach that the method can treat impotence or erectile dysfunction (instant claim 15) in males which can result from psychological disturbances (i.e. psychogenic; instant claim 17), physiological abnormalities in general (i.e. organic; instant claim 18), or for female sexual dysfunction (instant claim 16; see pg. 2, paragraphs 0037 and 0039-0040). Powders of apomorphine can also be used and placed in a capsule wherein the capsule is set in an inhalation device (instant claim 42; see pg. 3, paragraph 0047). The delivery device for inhalation may also include metered dose inhalers, dry powder inhalers or nebulization of solution or suspension (instant claims 19 and 42; see pg. 2, paragraph 0035). Apomorphine can exist as a free base or as an acid addition salt including the hydrochloride salt (instant claim 2; see pg. 3, paragraphs 0042-0043). Importantly, Gupta et al. teach that the apomorphine and its pharmaceutically acceptable salts thereof may be formulated into compositions together with one or more non-toxic physiologically tolerable or acceptable diluents, carriers, adjuvants or vehicle (instant

claim 1; see pg. 3, paragraph 0048). Of interest, Gupta et al. teach addition of adjuvants such as lecithin for maintaining proper fluidity (instant claims 24 and 26; see pg. 4, paragraph 0054). For solid dosage forms, powders may be formulated wherein the active compound may be mixed with at least one inert, pharmaceutically acceptable excipient or carrier including fillers such as lactose or lubricants such as magnesium stearate (instant claim 27; see pg. 4, paragraph 0055). Gupta et al. further demonstrated dose proportionate increase in both Cmax and in AUC (instant claims 7-9) and that administration by inhalation results in a more effective bioavailability without a proportional increase in adverse side effects (instant claim 10; see pg. 6, paragraph 0069). For the studies of the current invention, Gupta estimates that an 8 mg human dose is equivalent to about a 1.33 mg apomorphine dose in dogs (see pg. 7, paragraph 0074). Consequently, because administration of dosages in dogs in the range of 0.5 to 20mg/dog achieved plasma drug levels, an equivalent of 3 mg-120 mg human dose would also lead to plasma drug levels (i.e. 0.5 mg/dog x 8 mg human/1.33 mg dog; instant claims 11-14; see pg. 7, paragraph 0074).

Accordingly, the teachings of Gupta et al. anticipate claims 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 6, 12-14, 20-23, 25, and 28 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Gupta et al. (U.S. 2002/0006933 A1, previously cited by applicant and filed on an IDS 1449) as applied to 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42 in view of Lucas et al. (Pharmaceutical Research 1999, Vol. 16, No. 10, pgs. 1643-1647, cited by applicant and filed on an IDS 1449).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The Gupta reference is as discussed above and incorporated by reference herein. However, Gupta does not specifically teach a composition wherein the Cmax is achieved within 1 to 5 minutes or a terminal half-life of between 50 and 70 minutes or the exact dosages of apomorphine or additives in the composition. Similarly, Gupta et

al. does not teach that apomorphine has a mass median aerodynamic diameter of 10 microns or less.

Gupta does however teach that the Cmax is achieved immediately following administration necessarily meeting applicant's limitation of within 1 minute (see Gupta, pg. 7, paragraph 0072). As for the dosage limitation and terminal half-life, it is well within the purview of the skilled artisan vary the dosage of apomorphine and/or additives so as to obtain the most efficacious dosage in humans. Similarly, one of ordinary skill in the art would have found it obvious to optimize the dosage so as to obtain the best half-life of a dosage that is effective in treating sexual dysfunction.

Lucas et al. teach that an effective and efficient dry powder system for pulmonary delivery requires particles of mass median aerodynamic diameters that are in the range of 1.0-5 microns (see pg. 1643, abstract). For deep lung regions, even smaller aerodynamic diameters are preferred in the range of 1-2.0 microns (see pg. 1643, abstract). Importantly, Lucas et al. teach that dry powder inhalers (DPI) relies on both the formation of ordered units between the drug and the coarse carrier however efficiency is often poor (see pg. 1643, abstract). Thus, Lucas et al. teach that to avert the problems with poor flow, several solutions can be used including inclusion of excipient such as L-leucine which modifies the bulk properties of the formulation (see pg. 1643, abstract and pg. 1644, right col. and pg. 1646, rigt col.). For Preparation of powder aerosol formulation, Lucas et al. teach the use of an active such as salbutamol

sulphate using either a coarse or fine particles of lactose of 63-90 microns (instant claim 28; see pg. 1644, left col.).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to optimize the dosage and administer the composition of Gupta in the treatment of sexual dysfunction. Thus, given the teachings of Gupta and Lucas, one of ordinary skill would have been motivated to utilize the composition of Gupta and optimize the dosage of apomorphine and additives as taught by Lucas with the reasonable expectation of providing a composition that is effective in rapidly treating sexual dysfunction and composition that achieves high plasma levels.

While the exact dosages of the ingredients are not disclosed by Gupta et al., it is generally noted that differences in concentration do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or dosage is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or dosages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of ranges is the optimum combination of percentages.

Claims 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. 2002/0006933 A1) as applied to 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42 above and in further view of Vervaet et al. (International Journal of Pharmaceutics. 1999, Vol. 186, pgs. 13-30.).

The Gupta reference is as discussed above and incorporated by reference herein. However, Gupta does not teach a composition comprising a pMDI formulation with a propellant, water, and a solvent.

Vervaet et al. teach the current use of HFA 134 a and HFA 227 (instant claim 29-30 and 33-34) in pressurized metered dose inhalers (pMDI) along with co-solvents such as ethanol (pg. 21, left col.; instant claims 29 and 31) and surfactants and that the aforementioned propellants and excipients are particularly useful in stabilizing such suspensions and in enhancing the solubility of drugs (see pg. 13, abstract; pg. 20, left col. and pg. 24, left col.). However, for improved solubility of the drug, Vervaet et al. teach the addition of both HFA propellant and co-solvents (see abstract, pg. 13). Importantly, Vervaet teaches that due to the fact that surfactant solubility and drug solubility are heavily reliant on the ability to form dipole-dipole interactions between the solute and the liquid propellant, small amounts of competing dipolar molecules such as water can cause precipitation and thus strict control of water is required for co-solvents free HFA formulations (see pg. 19, left col., and right col., paragraph 2).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition of Gupta et al. in an MDI formulation and add propellants such as HFA 134a and HFA 227 along with ethanol and water since Gupta et al. teach that his composition can be formulated as an MDI and Vervaet et al. teach that HFA are the new alternatives to CFC propellants. Moreover, one of ordinary skill in the art would have found it obvious to add water in small amounts and optimize the concentration of the propellants since Vervaet et al. teach that water needs to be strictly controlled along with the amount of propellants for solubility purposes. Given the teachings of Gupta et al. and Vervaet, one of ordinary skill in the art would have found it obvious to add propellant, water, and ethanol with the reasonable expectation of providing a composition that is effectively administered in MDIs and a composition that is highly stable.

While the exact dosages of the ingredients are not disclosed by Vervaet et al., it is generally noted that differences in concentration do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or dosage is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or dosages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to

determine where in a disclosed set of ranges is the optimum combination of percentages.

Claims 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. 2002/0006933 A1) as applied to 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42 above and in further view of Pierre et al. (Annals of Allergy, Asthma and Immunology, April 1999, Vol. 82, No. 4, pgs. 377-382, abstract).

The Gupta et al. reference is as discussed above and incorporated by reference herein. However, Gupta does not particularly teach specific types of dry powder inhaler devices.

Pierre et al. teach the use of both propellant driven inhalers as well as breath actuated devices in treating asthma (see abstract). Importantly, Pierre et al. demonstrated that no significant differences existed in the potency and delivery system of the two devices (see abstract).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition of Gupta et al. as either an active inhaler or a breath actuated inhaler depending on the desired type of product and/or patient's preferences and ease of compliance. Given the teachings of Gupta et al. and Pierre, one of ordinary skill in the art would have found it obvious to select either an active inhaler or a breath actuated inhaler for the administration of the composition of Gupta et al. in the treatment of sexual dysfunction with the reasonable expectation of providing a

composition that is effectively administered in MDIs and a composition that is highly efficient in its delivery system.

Claims 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (U.S. 2002/0006933 A1) as applied to 1-2, 4-5, 7-11, 15-19, 24, 26-27, and 42 above and in further view of Snow (U.S. 2002/0134382 A1).

The Gupta et al. reference is as discussed above and incorporated by reference herein. However, Gupta does not particularly teach the use of a blister in the dry powder composition.

Snow teaches a medicament container configured to improve entrainment of the medicament in the air and to improve deposition of the medicament in the lungs (see abstract). Snow further teaches that several types of inhalation of devices exist and dry powder inhalers are one type of inhalation devices (see pg. 1, paragraph 0008). Snow further teaches that dry powder medicaments often relies on providing a package containing multiple doses of medicament wherein each is contained in a sealed blister (instant claim 45; see pg. 1, paragraph 0012). In fact, Snow teaches that the instant invention can comprise a blister type pack wherein the upper layer and bottom layer of the container is formed by a generally planar piece of material that may be readily punctured (see pg. 4, paragraph 0063 and pg. 5, paragraph 0076). Preferred embodiments include the upper layer formed by a piece of foil forming a disk and such

use of foil for blister packs is well known in the art and several types of foil are readily available (instant claim 46; see pg. 4, paragraph 0063). Moreover, Snow teaches that the lower layer can be formed of materials which are more durable than foil and be made of materials such as polypropylene that are compatible with the medicament being used (see pg. 5, paragraph 0077).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition of Gupta et al. as a blister pack since it is well-known in the art to formulate dry powder inhalers in blister pack and given that Snow teaches dry powder medications in foil blister packs for easy penetration by lancets. Moreover, one of ordinary skill in the art would have found it obvious to further formulate the disk with propylene containing layers since Snow teaches that such layers are compatible with the medicament. Given the teachings of Gupta et al. and Snow, one of ordinary skill in the art would have found it obvious to formulate the composition of Gupta et al. in a sealed blister pack and further include propylene layer for compatibility purposes with the reasonable expectation of providing a composition that is properly sealed and a container that is easily accessible.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

01/30/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617